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JEFF LLOYD
2421 N.W. 41ST STREET
SUITE A-1
GAINESVILLE, FL 32606-6669

EXAMINER	
LUCAS, ZACHARIAH	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 04/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

SM

Office Action Summary	Application No.	Applicant(s)	
	10/073,065	MOHAPATRA ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3 and 21-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3 and 21-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Currently, claims 3, 21-32 are pending and under consideration in the application.

2. Because this action raises new grounds of rejection not necessitated by amendment, it is being made Non-Final.

Specification

3. **(Prior Objection- Maintained)** The specification was objected to in the prior action as failing to provide proper antecedent basis for the claimed subject matter. See, 37 CFR 1.75(d)(1) and MPEP § 608.01(o). It is noted that Applicant appears to have interpreted this objection as a rejection under 35 U.S.C. 112,paragraph 1 for lack of written description. See, Response, page 1. This is not correct. The objection was merely on the basis that the specification does not provided antecedent support for subject presented in the claims. Correction of the following is required: The claims under examination read on immunogenic compositions comprising RSV either DNA or protein antigens. There does not appear, however, to be antecedent support for compositions comprising protein antigens. The paragraph inserted by the Applicant into the specification does not cure this problem because it refers merely to antigens, and not to protein antigens. As indicated in the prior action, due to the content of the remainder of the application, referring to the DNA vaccine as the antigen, the inserted paragraph does not provide adequate antecedent basis for compositions comprising protein antigens.

Claim Objections

4. **(Prior Objection – Withdrawn)** Claim 23 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. In view of the amendment of the claim, the objection is withdrawn.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. **(New Rejection)** Claims 3, and 21-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 3 is treated as representative. In the specification, the Applicant states that a plasmid DNA cocktail contains RSV antigens. See e.g., page 3, lines 10-15. However, the Applicant also indicates that the plasmids DNAs encode the antigens. Id, lines 9-10. Finally, the Applicant has argued in the response that they did not intend to change the meaning of the term antigen, and that the term reads on "substances that can stimulate an immune response and, given the opportunity, *react specifically by binding the effector molecules (antibodies) and effector cells (lymphocytes) produced.*" (Emphasis added). However, as described by the Applicant, the purpose of the DNA plasmids is not themselves to be antigens that fall within the scope of that definition, but to encode such antigens. Thus, it is unclear if the term "antigen" in claim 3 includes the DNA plasmids, or includes only the antigens encoded thereby.

In particular, it is unclear if, in claims 29-32, the Applicant intends the plasmid DNAs to act as the antigens of claim 3, or if the plasmid DNAs are present in the composition in addition to the antigens required to claim 3. This is because, if the term antigen as indicated in claim 3 is read so as to exclude the plasmid DNAs that do not themselves associate with "effector" molecules and cells, it appears that these claims require the presence of both plasmid DNAs and the encoded antigens. Further, if claims 29-32 do require the presence of both the antigens and plasmid DNAs, it is unclear how these claims differ from (e.g.) claim 27, which explicitly requires the presence of both the antigen and the DNA plasmids. Clarification is required.

7. **(New Rejection)** Claims 21-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims each depend from claim 3, which describes an immunogenic composition of claim comprising an M2 RSV antigen, an F and G antigen, and at least one other RSV antigen selected from an indicated group. Claim 21 further defines that the composition comprises one or more protein antigens encoded by one or more plasmid DNA. Claim 23 further indicates that the one or more plasmid DNAs are coacervated with chitosan to form nanospheres. Claim 21 does not indicate that the immunogenic compositions of claim 3 further include the DNA plasmids. However, claim 33 indicates that the DNA plasmids are coacervated into nanospheres. It is therefore unclear if the compositions of claims 21-23 includes both plasmids and the antigens indicated in claim 3, or if the claims are merely identifying the source of the antigens. Clarification is required.

8. **(New Rejection)** Claims 29 and 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 29 is treated as representative. This claim described the immunogenic composition of claim 3 "wherein said composition comprises one or more plasmid DNA encoding an M2 RSV polypeptide and at least three RSV polypeptides selected from the group consisting of F, G, M, SH, NSI, NS2, N, and P." It is unclear if the Applicant is requiring that the composition comprise at least one DNA encoding the M2 polypeptide, and also is requiring at least three polypeptides from the indicated group, or if the claim is requiring the presence of at least one DNA plasmid encoding the M2 polypeptide, and wherein said at least one DNA plasmid also encodes the at least three polypeptides selected from the group. Clarification is required.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. **(Prior Rejection- Withdrawn)** Claim 4 was rejected in the prior action under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claim read on an anti-RSV vaccine comprising an M2 RSV antigen and at least

one other RSV antigen. The claim was not enabled as the Applicant has not demonstrated that the claimed composition would be an effective vaccine against RSV infection. In view of the cancellation of this claim, the rejection is withdrawn.

11. **(New Rejection)** Claims 23, 26-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection. These claims read on immunogenic compositions comprising both an M2 polypeptide and a plasmid DNA encoding that protein, and both polypeptides and plasmid DNAs encoding polypeptides selected from the group of RSV F, G, M, NS1, NS2, N, and P polypeptides. Thus, this claim reads on compositions comprising both protein and plasmid DNA antigens. However, there is no written description support in the application for such a combination. Neither the written description nor the claims as filed provide support for such a combination. Rather, both the claims and the specification indicate that the Applicant intended the use of one or the other, but not of both polypeptides and plasmid DNAs. Thus, the indicated claims are rejected as adding new matter to the application.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. **(Prior Rejection- Withdrawn) Maintained under 35 U.S.C. 103(a))** Claims 3, 4, and 21-23 were rejected in the prior action under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Collins et al. (U.S. Patent 6,264,957, Collins I). The claims described immunogenic compositions comprising an RSV M2 antigen and at least one other RSV antigen. They have been amended however to require the presence of the M2, and at least 3 other antigens, among which may be the F G and N proteins. Because the amendment to the claims appears to avoid the rejection over Collins alone, the rejection is withdrawn.

14. **(New Rejection)** Claims 3, and 24, and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Murphy et al., U.S. Patent 5,882,651. These claims read on immunogenic compositions comprising at least the M2, the F, G, or N proteins. Murphy teaches immunogenic compositions comprising attenuated RSV particles. It is known in the art that the RSV virus comprises the proteins indicated in the claims. Because Murphy teaches immunogenic compositions comprising the virus, the reference anticipates the claims.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. **(Restatement of rejection over Collins et al.)** Claims 3, 4, and 21-23 were rejected in the prior action under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Collins et al. (U.S. Patent 6,264,957, Collins I). The claims described immunogenic compositions comprising an RSV M2 antigen and at least one other RSV antigen. They have been amended however to require the presence of the M2, and at least 3 other antigens, among which may be the F G and N proteins. The rejection is restated such that claims 3, and 21-24 are rejected as obvious over the teachings of Collins in view of Connors, J. Virol 65(3): 1634-37.

As indicated in the prior action, Collins teaches the making of an infectious RSV particle using plasmid vectors to express certain of the proteins. It is noted that the reference does not explicitly teach the making and use of particles comprising at least three of the antigens selected from the F, G, and N. However, the reference does teach the use of plasmids encoding the M2 and N proteins, the use of the resulting RSV particle as a vaccine itself (rather than as a vector for the expression of antigenic proteins). See e.g., column 3 lines 1-14, column 11 line 48 to column 12 line 8, and column 13, lines 15-30 (note that column 11 and 12 discuss use of the recombinant particle as the antigen itself, while column 13 teaches use of the particle as a vector for expression of the antigens). In addition to these teachings, the reference also teaches that additional plasmids, or on the same plasmids as used to encode the N, P, L, and M2 proteins, encoding other proteins may also be used to produce the RSV particles. Column 6 lines 5-13.

Thus, it would have been obvious to those in the art that additional antigens could be included in the RSV particles.

The F and G proteins are known to be effective immunogens against RSV, and because such proteins are known to also be located in the RSV membrane. See e.g., Connors, at 1634. It would therefore have been obvious to those in the art to include plasmids encoding these proteins such that they would be produced and incorporated into the resulting particles where the recombinant particles are intended for use as antigens against RSV infection. Because Collins teaches that other proteins may be incorporated into the RSV particles, and because the F and G proteins are known to be part of the viral capsid, those in the art would have had a reasonable expectation of success in the use of the plasmids to construct the RSV particles. Thus, the claims teach an immunogenic composition comprising antigens encoded by RSV polynucleotides in the form of plasmids.

17. **(Prior Rejection- Withdrawn)** Claims 3, and 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Collins et al. (PNAS 92: 11563-67, Collins II). These claims read on anti-RSV immunogenic compositions comprising an M2 antigen with at least one other RSV antigen. Collins II teaches the rescue of an infectious RSV particle from a cell transfected with plasmid cDNA encoding RSV N, P, L, and M2 proteins, and a cDNA encoding the antigenome of the virus. Page 11564. In view of the amendment to the claims requiring the presence of antigens other than those used in the Collins II reference, the rejection is withdrawn.

18. **(Prior Rejection- Withdrawn)** Claim 4 was rejected under 35 U.S.C. 103(a) as being unpatentable over Collins as applied to claim 3 above, and further in view of Wright et al. (J

Infect Dis 182(5): 1331-42). Claim 4 read on the immunogenic composition of claim 3, wherein the composition is a mucosal vaccine. In view of the cancellation of the claim, the rejection is withdrawn.

19. **(Prior Rejection-Withdrawn)** Claims 3, and 21-23 were rejected under 35 U.S.C. 103(a) as being unpatentable over Domachowske (supra) in view of the teachings of Hsu et al. (J Gen Virol 80: 1401-05) and Simmons et al. (J Immunol 166(2): 1106-13). The claims have been described above. The rejection is withdrawn in view of Applicant's arguments in traversal with respect to the Hsu reference, which was persuasive.

20. **(Prior Rejection- Withdrawn)** Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Domachowske in view of Hsu and Simmons as applied to claim3 above, and further in view of the teachings of Wyatt et al. (Vaccine 18: 392-97- of record in the May 2002 IDS). . In view of the cancellation of the claim, the rejection is withdrawn.

21. **(New Rejection)** Claims 3 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Conners et al., supra. Claim 3 merely requires the presence of certain antigens. Conners teaches that compositions comprising each of the RSV F, G, M2 and N antigens were effective at inducing an immune response. Because each of these antigens are disclosed as useful in inducing an immune response against RSV, it would have been prima facie obvious to combine the antigens in a single formulation. See e.g., MPEP 2144.06, and In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (each stating that it is per se obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose). The reference therefore renders obvious the claimed invention.

22. **(New Rejection)** Claims 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Conners in view of Cates et al., WO98/02457. These claims read on immunogenic compositions comprising RSV antigens. As described above, Conners teaches that the RSV M2, G, F, and N proteins are immunogenic. Cates teaches a composition comprising isolated proteins of the virus as antigens. Because Conners teaches that the M2, N, F, and G proteins are immunogenic, and because the Cates reference that immunogenic proteins may be used as antigens in a subunit RSV immunogenic composition, it would have been obvious to those in the art to have made such a vaccine with the antigens described in Conners. Because the isolated proteins would be structurally identical to the proteins encoded by the plasmids indicated in the rejected claims, the references render obvious the claimed invention.

23. **(New Rejection)** Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Conners as applied to claims 3 and 24 above, and further in view of Domachowske et al., Clin Microbiol Rev 12(2): 298-309. Claim 25 requires the presence of each of the listed antigens, all of which are known proteins of the RSV particle. Conners teaches that each of the N, M2, F, and G proteins are effective at inducing neutralizing immune responses to RSV infection. Other proteins are disclosed as targets for immune responses by Domachowske. It would therefore have been obvious to those in the art to combine these antigens to induce an immune response to RSV.

24. **(New Rejection)** Claims 3 and 24-27, 29, 30, and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Conners as applied to claim 3 above, and further in view of the teachings of Li et al. (J Exp Med 188(4): 681-88) and Li et al. (Virology, 269: 54-65) and in light of the teachings of Montgomery et al., Phamacol Ther 74(2): 195-205). The claims have been described above, as have the teachings of Connors. For the purposes of this rejection, claim 27 is interpreted as reading on compositions of both antigens and plasmid DNA, claims 24-26 as reading on compositions comprising only polypeptide antigens, and claims 29, 30, and 32 as requiring only the presence of the indicated plasmid DNAs.

Conners teaches several RSV proteins that are capable of inducing an immune response against RSV. Each of the Li references indicates that use of plasmid DNA vaccines encoding antigens of the virus leads to an improved immune response to those seen with other vaccines, and a response comparable to that seen with natural RSV infection. In addition to the teachings of the Li references demonstrating the efficacy of DNA vaccines with the RSV F and G antigens, it was known in the art that DNA plasmid vaccines generally provide several advantages over the use of other vaccines known in the art. See e.g., Montgomery, page 202. It would therefore have been obvious to those in the art to combine the teachings of the Connors and Li references such that a plasmid DNA vaccine encoding at least the M2, G, F, and N proteins was made. Further, because the art teaches both the use of plasmid DNA compositions and RSV polypeptide antigen compositions to induce immune responses against RSV, it would have been prima facie obvious to combine such compositions as required by claim 27. See e.g., MPEP 2144.06, and In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (each stating that it is per se obvious to combine two compositions each of which is taught by the prior art to be useful for the

same purpose). The teachings of Conners and the Li references therefore render obvious the claimed inventions.

25. **(New Rejection)** Claims 28 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Conners in view of the teachings of the Li references, and further in view of Leong et al., J Controlled Release 53: 183-93. The teachings of Conners and Li have been described above. While these references teach the making and use of DNA plasmid compositions encoding RSV antigens, the references do not teach the coacervation of the plasmids with chitosan. However, Leong teaches that such coacervation can improve the delivery of plasmid DNAs into cells. Thus, it would have been obvious to those in the art to combine the teachings of Leong with those of the other references to coacervate the RSV antigen encoding plasmids with chitosan for inclusion in an immunogenic composition. The references therefore render the claims obvious.

Conclusion

26. No claims are allowed.

27. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner

4/2/04

JAMES HOUSEL
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600